HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

APPENDIX

ROBUST SUMMARY

FOR

ISODECYL BENZOATE

(CAS Nos. 131298-44-7)

Submitted to the U.S. EPA

By

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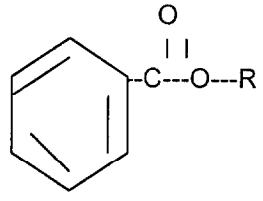
November 13, 2001

CONTENTS

SIDS PROFILE

DATE: November 9, 2001

1.1 A.	CAS No.	131298-44-7
1.1 B.	CHEMICAL NAME	ISODECYL BENZOATE
1.1 C.	MOLECULAR WEIGHT	262 (predominant component)
1.1 D, E.	FORMULA & STRUCTURE	$C_{17}H_{26}O_2$  where R = C9-11 branched alkane
1.5	QUANTITY	Approx. 1.5MM#/yr.
1.7	USE PATTERN	Plasticizer for caulks, sealants and adhesives.
1.9	SOURCES AND LEVELS OF EXPOSURE	Limited due to use in primarily closed systems.
TEST PLAN JUSTIFICATION /ISSUES FOR DISCUSSION	SIDS testing required: In the area of "Environmental Fate and Pathways": • Photodegradation • Stability in water • Transport and distribution	

Tier 1
SIDS SUMMARY

Date: November 9, 2001

CAS NO: 131298-44-7		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	SIDS Testing Required
STUDY		**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
PHYSICAL CHEMICAL DATA								
2.A	Freezing Point	Y	Y	Y		N	Y	N
2.B	Boiling Point	Y	Y	Y		N	Y	N
2.C	Density	Y	Y	Y		N	Y	N
2.D	Vapor Pressure	Y	Y	Y		N	Y	N
2.E	Partition Coefficient	Y	Y	Y		N	Y	N
2.F	Water Solubility	Y						N
2.G	Flash Point	Y						N
2.H	Auto Flammability	Y						N
2.I	Flammability	Y						N
2.J	Explosive Properties	Y						N
2.K	Pyrophoricity	Y						N
2.L	Oxidation: Reduction Potential	Y						N
ENVIRONMENTAL FATE and PATHWAY								
3.A	Photodegradation	N					Y	Y
3.B	Stability in Water	N					Y	Y
3.D	Transport and Distribution	N					Y	Y
3.E	Biodegradation	Y	Y	Y		N	Y	N
ECOTOXICITY								
4.A	Acute Toxicity to Fish	Y	Y	Y		N	Y	N
4.B	Acute Toxicity to Daphnia	Y	Y	Y		N	Y	N
4.C	Toxicity to Algae	Y	Y	Y		N	Y	N
TOXICITY								
5.A	Acute Toxicity							
5.A.1	* Acute Oral	Y	Y	Y			Y	N
5.A.2	* Acute Inhalation	Y	Y	Y			Y	N
5.A.3	* Acute Dermal	Y	Y	Y			Y	N
5.D	Repeated Dose (General)	Y	Y	Y	Y		Y	N
5.E	Genetic Toxicity *in vitro*							
	* Gene Mutation	Y	Y	Y			Y	N
	* Chromosomal Aberration	Y	Y	Y			Y	N
5.F	Genetic Toxicity *in vivo*	Y	Y	Y			Y	N
5.H	Reproduction Toxicity	Y	N	Y	Y		Y/N	N
5.I	Developmental Toxicity/Teratogenicity	Y	Y	Y			N	N

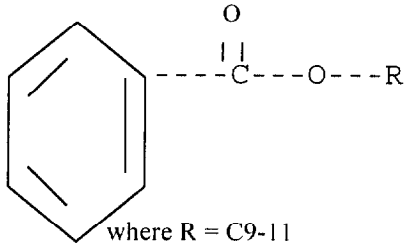
1.0 GENERAL INFORMATION

1.01 OECD AND COMPANY INFORMATION

Velsicol Chemical Corporation
10400 West Higgins Road
Suite # 600
Rosemont, Illinois 60018
USA

1.1 SUBSTANCE INFORMATION

A. CAS Number: 131298-47-7
B. OECD Name: Isodecyl Benzoate
C. Molecular Weight: 262 (predominant component)
D. Molecular Formula: $C_{17}H_{26}O_2$
E. Structural Formula:



where R = C9-11 branched alkane

F. Type of Substance: Organic [X]
G. Physical State: Liquid [X]

1.2 SYNONYMS:

Benzoic Acid, C9-11 branched alkyl esters

C9-11 branched alkyl benzoate

Velate™ 262

Plasticizer 262

Benzoflex™ 131

1.3 IMPURITIES:

Toluene < 1%

Benzoic Acid < 1%

1.5 QUANTITY

Between 1.5 and 1.6 million pounds of isodecyl benzoate have been sold in both 1999 and 2000.

1.7 USE PATTERN

A. General
Isodecyl benzoate is used industrially in latex caulks.
It also has applications in sealants and adhesives.

B. Uses in Consumer Products
Caulks, sealants and adhesives sold to consumers may contain a small amount of isodecyl benzoate.

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES – None established

1.9 SOURCES OF EXPOSURE

The manufacturing process used to produce isodecyl benzoate is essentially a closed system with no routine source of worker exposure. Exposure may occur during non-routine tasks such as maintenance or during process upsets. Exposure measurements of isodecyl benzoate have not been made during the manufacturing of this material nor during the manufacturing of paints, caulks, sealants and adhesives. Exposure to small amounts of isodecyl benzoate may occur during the application of the final paint formulation, caulk, sealant or adhesive as part of the normal drying process.

2. PHYSICAL/CHEMICAL DATA

A. FREEZING POINT

Value: <-25 °C (<248.15 K)

Test Substance: 98.2% Purity

Method: EEC Methods for the Determination of Physicochemical Properties, Directive 92/60/EEC (OJ No. L383A 29.12.92), Part A, Method A1.

GLP: Yes [X] No [ ] ? [ ]

Remarks: The test was performed in duplicate.

Reliability: [1] Valid without Restriction

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties. " Report No. VCL 217/943240, pp.11-15, October 10, 1995.

B. BOILING POINT

Value: 321.5 to 342.5°C

Test Substance: 98.2% Purity

Pressure: 1013 mbar

Decomposition: The last remaining drops in the flask decomposed to a black solid, probably due to excessive local heating.

Method: EEC Methods for the Determination of Physicochemical Properties, Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A, Method A2.

GLP: Yes [X] No [ ] ? [ ]

Remarks: The test was performed in duplicate using a fresh sample each time. The boiling range was determined using a reduced-scale distillation method, due to the high boiling point of the material. In the boiling range, the distillate collected in each test (30ml) appeared to be the same as the original liquid

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943240, pp.16-19, October 10, 1995.

C. **DENSITY**

Type: Relative Density

Test Substance: 98.2% Purity

Value: 0.95155

Temperature: 20/4°C

Method: "EEC Methods for the Determination of Physicochemical Properties," Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A, Method A3.

GLP: Yes [**X**] No [ ] ? [ ]

Remarks: The test was performed in duplicate using the pycnometer method as described in ISO Recommendation R1183.

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943240, pp.20-22, October 10, 1995.

D. **VAPOR PRESSURE**

Test Substance: 98.2% Purity

Value: 8.45×10^{-3} Pascals

Temperature: 25 °C

Method: Measured using a vapor pressure balance method in accordance with EEC Directive G7/548, Annex V, Method A4, as published in 92.69/EEC and the Health and Safety Commissions Approved Code of Practice, Test A4.

GLP: Yes [**X**] No [ ] ? [ ]

Remarks: None

Reliability: [1] Valid without Restrictions

Reference: Taylor, N. "Determination of Vapor Pressure by Balance Method: Isodecyl Benzoate", Project No. VCL 217, University of Leeds, Leeds LS29JT, England, March 1995.

E. PARTITION COEFFICIENT

Test Substance: 98.2% Purity

Value: Log K_{ow} = 4.61

Temperature: 21°C

Method: Measured by a flask-shaking method as described in "EEC Methods for Determination of Physicochemical Properties," Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A, Method A8.

GLP: Yes [X] No [ ] ? [ ]

Remarks: Isodecyl Benzoate was dissolved in and made to volume (200ml) with water-saturated octanol to give a stock solution of concentration 2537 mg/ml. Then, either 10, 20 or 40 ml of this stock solution was mixed with octanol-saturated water (110ml) and shaken mechanically for 15 minutes. Each stock solution volume was tested in duplicate. The test phases were separated by centrifugation, transferred to separating funnels, and then analyzed by HPLC. A mean value of 4.61($Log_{10}Po_w$) was determined to be the partition coefficient for isodecyl benzoate

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemcial Properties." Report No. VCL 217/943/240, pp.32-47, October 10, 1995.

F. WATER SOLUBILITY

Test Substance: 98.2% Purity

Value: $<0.686 \times 10^{-4}$ g/L

Temperature: 20°C

Description: [X] of very low solubility

Method: Determined by the flask-stirring method in accordance with the "EEC Methods for the Determination of Physicochemical Properties ," Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A, Method A6.

GLP: Yes [X] No [ ] ? [ ]

Remarks: The analytical data showed that the water solubility of isodecyl benzoate was less than the detection limit (three times the baseline noise) which was calculated as 0.068567 ug/ml. The pH ranged from 4.38 to 5.98.

Reliability: [1] Valid without Restriction

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943/240, pp.23-31, October 10, 1995.

G. FLASH POINT

Test Substance: 98.2% Purity

Value: 110°C

Type: Closed Cup

Method: Determined using the Pensky-Martens closed-cup method as described in ASTM D93-80 and in accordance with "EEC Methods for the Determination of Physicochemical Properties," Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A, Method A9, except that a resistance thermometer was used for a sample temperature measurement.

GLP: Yes | **X** | No | | ? | |

Remarks: The test was run in duplicate. The atmospheric pressure at the time of the test was 1030 mbar.

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate : Physicochemical Properties." Report No. VCL 217/943/240, pp.48-50, October 10, 1995.

H. AUTOFLAMMABILITY (IGNITION)

Test Substance: 98.2% Purity

Result: The auto-ignition temperature of isodecyl benzoate was determined to be 374°C.

Method: As described in ASTM-E-G59-78 and in accordance with "EEC Methods for the Determination of Physicochemical Properties," Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A Method A15.

Remarks: The test was run in duplicate at a barometric pressure of 1037 mbar.

Reliability: [1] Valid without restrictions

GLP: [X] Yes [ ] No [ ] ?

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943/240, pp.60-64, October 10, 1995.

I. FLAMMABILITY

Type: Contact with water

Test Substance: 98.2% Purity

Result: No gas was evolved during any of the test. Isodecyl benzoate was not considered to be flammable.

Method: "EEC Methods for the Determination of Physicochemical Properties," Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part A Method A12.

Remarks: None.

GLP: [X] Yes [ ] No [ ] ?

Reliability: [1] Valid without restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943/240, pp.51-52, October 10, 1995.

J. EXPLOSIVE PROPERTIES

Test Substance: 98.2% Purity

Result: Not explosive.

Method: A Koenen test apparatus for thermal sensitivity (effect of a flame) and a fall hammer for determination of mechanical sensitivity (shock) were used in accordance with "EEC Methods for the Determination of Physicochemical Properties," Directive 92/69/EE (OJ No. L383A, 29.12.92), Part A Method A14.

Remarks: The test substance ignited in each test, but no explosions or deformation to any of the tubes were observed; therefore, isodecyl benzoate is not explosive.

GLP: [X] Yes [ ] No [ ] ?

Reliability: [1] Valid without restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943/240, pp.55-59, October 10, 1995.

K. PYROPHORICITY

Test Substance: 98.2% Purity

Results: Not pyrophoric (Isodecyl benzoate does not ignite after being brought into contact with air at a temperature of 25 °C plus or minus 10°C within a 5-minute period.)

Method: "EEC Methods for the Determination of Physicochemical Properties," Directive 92/G9/EEC (OJ No. L383A, 29.12.92), Part A, Method A13.

Remarks: At a test temperature of 19°C, the test substance gave negative results six times in the Drop Test and three times in the Char Test. Under the conditions of this study, it was not considered to be pyrophoric.

GLP: [X] Yes [ ]No [ ] ?

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre. "Isodecyl Benzoate: Physicochemical Properties." Report No. VCL 217/943/240, pp. 53-54, October 10, 1995.

L. OXIDATION:REDUCTION POTENTIAL – Not Determined

3. ENVIRONMENTAL FATE AND PATHWAYS

A. **PHOTODEGRADATION** – No Information

B. **STABILITY IN WATER** – No Information

C. **MONITORING DATA (ENVIRONMENT)** – No Information

D. **TRANSPORT AND DISTRIBUTION** – No Information

E. **BIODEGRADATION**

(1) Preferred Result

Type: Aerobic

Inoculum: Activated sewage sludge bacteria

Concentration of the Test Substance: 2 mg/L

Degradation: 20% after 28 days

Kinetics: 0% at 1-4 days, ~20% after 10 days; 20% after 28 days

Method: In accordance with OECD Guideline No. 301D, Ready Biodegradability: Closed Bottle Test, 1981.

Test Substance: Isodecyl benzoate at a purity of >98% active ingredient

Test Conditions: Sealed bottles containing the test substance (adsorbed onto glass filter paper) and inorganic nutrient medium were inoculated with activated sewage sludge bacteria and incubated up to 28 days at 20°C. On days 0, 4, 7, 11, 14, 18, 21, 25 and 28, duplicate bottles were taken and dissolved oxygen measurements were performed electrochemically. Percentage biodegradation values were determined by comparing the extent of oxygen depletion with the Theoretical Oxygen Demand (2.75 mg O_2/mg). Additional bottles containing both the test substance and a readily biodegrable standard substance were prepared in order to provide additional information on the inhibitory \ effect of the test substance.

Results: Isodecyl benzoate attained only 20% biodegradation after 28 days and cannot, therefore, be termed as biodegradable. Cultures containing both test and standard substances combined showed an oxygen value 36% higher than that anticipated on the basis of results from separate cultures on Day 14. Consequently, isodecyl benzoate is not considered to have had an inhibitory effect on sewage bacteria under conditions of this test. Oxygen depletion in the inoculated control series was within prescribed limits (<1.5 mgO_2/L after 28 days).

GLP: Yes [X] No [ ] ? [ ]

Remarks: Isodecyl benzoate was not found to be inhibitory to activated sewage sludge bacteria under the conditions of this test.

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre, Ltd. Isodecyl Benzoate: Ready Biodegradability (Closed Bottle Test), Report No. VCL 218 (b)/950109, April 27, 1995.

(2) Supporting Data

Type: Aerobic

Inoculum: Activated sludge at 30 mg/L as the concentration of suspended solid

Concentration of Test Substance: 100 mg/L

Degradation: Mean of 67% at 28 days

Kinetics: 26% biodegradation by BOD at 7 days.
56.7% biodegradation by BOD at 14 days
63.7% biodegradation by BOD at 21 days
67% biodegradation by BOD at 28 days

Method: In accordance with OECD Guideline No. 301C, Ready Biodegradability: Modified MITI Test, May 12, 1981.

Test Substance: Isodecyl benzoate at a reported purity of 100%.

Test Conditions: The concentration of the test substance was 100 mg/L and the concentration of activated sludge was 30 mg/L (as the concentration of suspended solid). The volume of the test solution was 300 ml. Cultivation took place at a temperature of 25°C for a period of 28 days. BOD was measured by a closed-system oxygen consumption apparatus.

Results: At the initiation of cultivation, test substance was not dissolved in vessels containing water and test substance or sludge and test substance. At the completion of cultivation, test substance was still not dissolved in the vessel containing water and test substance; however, in the vessel containing sludge and test substance, the test substance was now not apparent and growth of the sludge was observed. Biodegradation by BOD after 28 days averaged 67 % (3 replicates), indicating that isodecyl benzoate was "readily biodegradable" under the conditions of this study.

GLP: Yes [X] No [ ] ? [ ]

Remarks: Isodecyl benzoate was readily biodegradable under the conditions of this particular study. Its percentage biodegradability by BOD was 67% after 28 days.

Reliability: [2] Valid with Restrictions

Reference: Kurume Research Laboratories Test on Biodegradability of Benzoflex^{R} 131 by Microorganisms, Test No. 11901, March 13, 1991.

F. ADDITIONAL STUDY

Type: Aerobic (Respiration Inhibition Study)

Inoculum: Activated sewage sludge incubated with synthetic sewage

Concentration of Test Substance: 100 mg/L

Result: The EC50 (respiration inhibition) was >100 mg/L for a 3-hour contact time.

Method: In accordance with OECD Guideline No. 209 and EEC Methods for the Determination of Ecotoxicity, EEC Directive 67/548, Annex VIII, Part C (87/302/EEC), Activated Sludge, Respiration Inhibition Test

Test Substance: Isodecyl benzoate at a purity of >98% active ingredient.

Test Conditions: Cultures of activated sewage sludge were incubated with synthetic sewage under vigorous aeration and in the presence of the test substance. Aeration was interrupted after 3 hours and the rates of respiration were measured electrochemically for each culture. Percent inhibition of respiration was calculated for each culture after a 3-hour contact period by comparing a oxygen depletion rates for the test substance with those for the solvent control culture. A positive control (3,5-dichlorophenol) was used to demonstrate the satisfactory performance of the procedure.

Results: The 3-hour EC50 (for respiration inhibition) was >100 mg/L for isodecyl benzoate compared to 6.5 mg/L for the positive control (3,5-dichbrophenol), using activated sewage sludge.

GLP: Yes [X] No [ ] ? [ ]

Remarks: A test substance concentration of 100 mg/L was the highest test concentration that could be prepared due to limited solubility in water. It was also considered unnecessary and unrealistic to test at concentrations in excess of 100 mg/L

Reliability: [1] Valid without Restrictions.

Reference: Huntingdon Research Centre, Ltd. Isodecyl Benzoate: Inhibitory Effect on the Respiration of Activated Sewage Sludge, Report No. VCL 218(a)/941210, April 27, 1995.

4. ECOTOXICITY

A. ACUTE TOXICITY TO FISH

Type of Test: Static [ ] Semi-static [ ] Flow through [X]

Species/strain: *Oncorhyncus mykiss* (rainbow trout)

Exposure period: 96 hours

Results: 96-hour LC50 >6.5mg/L
NOEC=6.5mg/L
No Mortality Concentration=6.5mg/L

Method: In accordance with OECD Guideline 203 and the Council of European Communities Directive 67/548/EEC, Annex 5, Guideline C.1

Test Substance: Isodecyl benzoate with a purity of 98% active ingredient

Remarks: A nominal concentration of 100mg/L of isodecyl benzoate was used for the study, a value much greater than the estimated solubility limit (50 ug/L). Observations of both the mixing chambers and test chambers showed an oily film on the surface of the test solutions even though a solvent concentration of 0.1ml/l was provided. Diluter operations functioned properly. Therefore, the test concentration measured was the highest that could be attained (6.5 mg/L) based on the water solubility of the test substance. No mortality, adverse clinical signs or abnormal behavior were observed during the 96-hour exposure period.

GLP: Yes [X] No [ ] ? [ ]

Reliability: [1] Valid without Restrictions

Reference: Wildlife International Ltd. "Isodecyl Benzoate: A 96-Hour Flow-Through Acute Toxicity Test with the Rainbow Trout." Project No. 107A-105, January 24, 1995.

B. ACUTE TOXICITY TO INVERTEBRATES

Type of Test: Static [X] Semi-static [ ] Flow-through [ ]

Species/strain: *Daphnia magna*

Exposure period: 48 hours

Results: 48-hour EC50=0.54 mg/L (0.46-0.70 mg/L CL)
NOEC=0.089 mg/L
No Mortality Concentration=0.28 mg/L

Method: In accordance with OECD Guideline 202 and the Council of European Communities Directive 67/548/EEC, Annex V, Guideline C.2

Test Substance: Isodecyl benzoate with a purity of 98% active ingredient

Analytical Monitoring: Yes (HPLC with UV Detection)

Remarks: A negative control, a solvent control, and isodecyl benzoate measured concentrations of 0.089, 0.11, 0.28, 0.46 and 0.70 mg/L were used. Mean measured test concentrations were determined from samples of test water collected from one replicate of each treatment and control group at the beginning of the test and at test termination. Deaths occurred at the two highest exposure levels and the 48-hour EC50 was calculated to be 0.54 mg/L.

GLP: Yes [X] No [ ] ? [ ]

Reliability: Valid with Restrictions-
(At 48 hours, less than 50% of the test substance remained in the aquaria.
However, all measured test levels were above the reported solubility limit of isodecyl benzoate (50ug/L) and therefore, these study results should be adequate to evaluate the toxicity of the compound to *Daphnia magna*

Reference: Wildlife International Ltd. "Isodecyl Benzoate: A 48-Hour Static Acute Toxicity Test with the Cladoceran (*Daphnia magna*). Project No. 107A-104, January 24, 1995.

C. ACUTE TOXICITY TO AQUATIC PLANTS (ALGAE)

Type of Test: Static [X] Semi-static [ ] Flow through [ ]

Species/strain: *Selenastrum capricornutum* (freshwater alga)

Exposure period: 96 hours

Endpoint: Growth rate and cell density

Results:

a. Cell Density
   96-hour EC10 >50ug/L
   96-hour EC50 >50ug/L
   96-hour EC90 >50ug/L
b. Growth Rate
   96-hour EC10 >50ug/L
   96-hour EC50 >50ug/L
   96-hour EC90 >50ug/L

Method: In accordance with procedures outlined in Title 40 of the US Code of Federal Regulations, Part 797, Section 1050, "Algal Acute Toxicity Test" and "Short-Term Methods for Estimating the Chronic Toxicity of Effluents and Receiving Waters to Freshwater Organisms; consistent with OECD guidelines.

Test Substance: Isodecyl benzoate at a purity of 98% and a water solubility of < 1ug/mL

Analytical Monitoring: Yes (HPLC with UV detection)

Remarks: In this study, green algae were exposed to a negative control, a positive control, and mean measured concentrations of isodecyl benzoate of 6.1, 16 and 50ug/L. Cell density and growth rate were determined at 24 -hour intervals. There were no statistically significant effects on mean cell density or cell growth in any test group. Therefore, the EC10, EC50 and EC90 were all >50 ug/L. At each concentration, analytical measurements were taken at test initiation (0 hour) and after 96 hours. The two lowest of 5 initial nominal test concentrations were dropped because the analytical concentration of test substance was below the limit of analytical detection.

GLP: Yes [**X**] No [ ] ? [ ]

Reliability: [2] Valid with Restrictions
(only three test concentrations)

Reference: Wildlife International Ltd. "Isodecyl Benzoate: A 96-Hour Toxicity Test with the Freshwater Alga (*Selenastrum capricornutum*). Project No. 107A-101, January 25, 1995.

D. CHRONIC TOXICITY TO FISH

Type of Test: Static [ ] Semi-static [ ] Flow-through [X]

Species: *Pimephales promelas* (fathead minnow)

Endpoint: Early life-stage development indices such as time to hatch, hatching success, survival and growth

Exposure Period: 33 days

Analytical Monitoring: Yes (at each concentration on days 0, 7, 14, 21 and 28 by HPCL with UV detection)

Method: This early life-stage toxicity test with fathead minnow embryos was based on procedures outlined in the Code of Federal Regulations, Part 797, Section 1600, "Fish Early Life-Stage Toxicity Test; and ASTM Standard E 1241-88, "Standard Guide for Conducting Early Life-Stage Toxicity Tests with Fish." Fathead minnow embryos were exposed to a negative control, a solvent control, and 5 nominal concentrations of 0.81, 2.7, 9.0 30 and 100 ug/L of isodecyl benzoate for 33 days (a 5-day embryo hatching period plus a 28-day post-hatch juvenile growth period).

Test Substance: Isodecyl benzoate with a purity of 98% active ingredient

Results: There were no adverse effects on hatching process, survival or growth of fathead minnows at any test concentration. The NOEC was 100 ug/L nominal (47 ug/L mean measured concentration). The lowest observed effect concentration (LOEC) was not determined in this test because no adverse effects were seen at any test concentration. The LOEC and the maximum acceptable toxicant concentration (MATC) could be considered greater than 47 ug/L isodecyl benzoate.

Remarks: Analytical samples collected from the controls and the 3 lowest treatment groups were below the limit of quantification (LOQ), 6 ug/L, while samples collected from the 2 highest treatment groups showed measured concentrations of 13 ug/L and 47 ug/L, respectively.

GLP: [X] Yes [ ] No [ ] ?

Reference: Wildlife International Ltd. "Isodecyl Benzoate: An Early Life-Stage Toxicity Test with the Fathead Minnow." Project No. 107A-102, January 24, 1995.

E. CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of Test: Static [ ] Semi-static [ ] Flow-through [X]

Species: *Daphnia magna*

Exposure Period: 21 days

Endpoints: Survival, growth and reproductive indices of *Daphnia magna* over a 21-day exposure period under flow-through test conditions

Exposure Period: 21 days

Analytical Monitoring: Yes (at each concentration on days 0, 7, 14 and 21 by HPCL with UV detection)

Method: The protocol for this study was based on procedures outlined in Title 40 of the Code of Federal Regulations, Part 797, Section 1330, "*Daphnia* Chronic Toxicity Test"; and ASTM E 1193-87, "Standard Guide for Conducting Renewal Life-Cycle Toxicity Tests with *Daphnia magna*." Daphnids were exposed to a negative control, a solvent control and 5 selected nominal concentrations of isodecyl benzoate (0.81, 2.7, 9.0, 30 and 100 µg/L) for 21 days.

Test Substance: Isodecyl benzoate at a purity of 98% active ingredient

Results: No adverse effects on survival, reproduction or growth of *Daphnia magna* were seen in the solvent control or at any test concentration of isodecyl benzoate. The NOEC was 100 g/L nominal (39 ug/L mean measured concentration), the highest concentration tested. No LOEC was determined since no adverse effects were seen at any test concentration. The LOEC and the maximum acceptable toxicant concentration (MATC) could be considered greater than 39 µg/L for isodecyl benzoate.

Remarks: Each treatment and control group were run in duplicate. Samples collected from the control and the 3 lowest test concentrations were below the limit of quantification (LOQ), 6.0 g/L, while samples collected from the 2 highest treatment groups showed values of 10 g/L and 39 g/L for isodecyl benzoate, respectively.

GLP: [X] Yes [ ] No ?[ ]

Reference: Wildlife International Ltd. "Isodecyl Benzoate: A Flow-Through Life-Cycle Toxicty Test with the Cladoceran (Daphnia magna). Project No. 107A-103, January 24, 1995.

5. TOXICITY

A. ACUTE TOXICITY

(1) Acute Oral Toxicity

Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [**X**]; LDL_0 [ ]; Other [ ]

Species/strain: Sprague-Dawley Rats

Value: >5000 mg/kg

Method: In accordance with 1982 EPA Guideline (Guideline 81-1, 1982) and consistent with OECD Guideline 401, five male and 5 female rats were dosed by gavage with the undiluted material at a concentration of 5000 mg/kg body weight, observed for 14 days post-dosing, and then given a gross pathological examination.

GLP: Yes [**X**] No [ ] ? [ ]

Test substance: Isodecyl benzoate, unknown purity

Remarks: No mortality occurred during dosing or during a 14-day post-dosing period. Two males and 2 females had diarrhea 4 hours after dosing. All males and females showed a yellow-stained genital region at 1 and 2 days after dosing. No other adverse clinical signs were seen.

Reliability: [2] Valid with Restrictions

Reference: Hazleton Laboratories America, Inc. "Acute Oral Toxicity Study of Isodecyl Benzoate in Rats." Report No. HLA 70504073, August 25, 1987.

(2) Acute Inhalation Toxicity

Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [**X**]; LCL_0 [ ]; Other [ ]

Species/strain: Sprague-Dawley Rats

Value: Male Rats 3.9 mg/L (2.8 to 5.6 mg/L CL)
Female Rats 2.0 mg/L (1.1 to 3.4 mg/L CL)
M & F Rats 3.3 mg/L (2.2 to 4.9 mg/L CL)

Method: Consistent with OECD Guideline No. 403. Three groups of 5 rats/sex were exposed to isodecyl benzoate as a respirable aerosol for 4 hours at target exposure levels of 1, 3 and 5 mg/L, respectively, observed for a 14-day post-exposure period, and then subjected to a gross pathological examination. Isodecyl benzoate was generated as a respirable aerosol in the breathing zone of the rats. Five to six times during each exposure, chamber atmospheres were sampled for gravimetric determination of the test material concentration. Aerosol particle size distribution was assessed by sampling a measured volume of test atmosphere through a cascade impactor twice during each exposure. Chamber temperature and relative humidity were also monitored continuously during each exposure. The exposure vessel was a 100-liter plexiglass chamber, operated in a dynamic mode, with total airflow through the chamber of 21.1 liters per minute.

GLP: Yes [**X**] No [ ] ? [ ]

Test substance: Isodecyl benzoate with a purity of 95+% active ingredient

Remarks: Mean analytical concentrations (plus or minus one standard deviation) for the 3 exposure levels were 1.0 plus or minus 0.085 mg/L, 2.98 plus or minus 0.232 mg/L, and 5.18 plus or minus 0.926 mg/L. Mortality occurred only at the 2.98 mg/L level (0/5 M, 4/5 F) and the 5.18 mg/L level (5/5 M and 5/5 F). For the 3 test levels, mass median aerodynamic diameter (MMAD) of the aerosol ranged from 3.12 to 3.34 microns. Adverse clinical signs at all test levels included languid behavior, rough haircoat, dyspnea, polypnea, squinting, tremors and hunched appearance during exposure. Up to one hour post-exposure, respiratory distress, eye irritation, and urine-stained fur were also observed. Between 50 minutes and 5 days post-exposure, mortalities occurred at the mid- and high-test levels. During the 2nd post-exposure week, all survivors appeared normal except for incidences of sores and alopecia.

Reliability: [1] Valid without Restrictions

Reference: Hazleton Laboratories of America, Inc. "Acute Inhalation Toxicity Study with Isodecyl Benzoate in the Rat." Report No. HLA 686-167, May 6, 1998.

(3) Acute Dermal Toxicity

Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [**X**]; LDL_0 [ ]; Other [ ]

Species/strain: New Zealand White Rabbits (males and females)

Value: >2000 mg/kg bodyweight

Method: According to US EPA Guideline for Testing Pesticides and Toxic Substances, Guideline 81-2, 1982, and consistent with OECD Guidelines. Five male and five female rabbits were dermally exposed to isodecyl benzoate at a dose of 2 g/kg bodyweight for 24 hours. After removal of the patches and cleansing of the skin, rabbits were observed for mortality and adverse clinical signs (1st four hours). Evaluation of dermal irritation was done at 30 minutes, day 3, day 7, day 10 and day 14 post-exposure. During the 14-day post-exposure period, animals were examined for adverse clinical signs twice daily; bodyweights were measured at day 0, 7, and 14 days post-exposure. A gross pathological examination was conducted on all animals at termination of the study.

GLP: Yes [**X**] No [ ] ? [ ]

Test substance: Isodecyl benzoate, purity unknown

Remarks: No mortality or adverse clinical signs occurred during the study. The estimated dermal LD50 for male and male rabbits was greater than 2000 mg/kg of bodyweight. Dermal irritation consisted of slight-to-moderate edema, erythema and desquamation, and slight atonia, coriaceousness and fissuring

Reliability: [1] Valid without Restrictions

Reference: Hazleton Laboratories of America, Inc. "Acute Dermal Toxicity Study of Isodecyl Benzoate in Rabbits." Report No. HLA 7050474, August 25, 1987.

B. CORROSIVENESS AND IRRITATION

(1) Skin Irritation

Type: Primary Dermal Irritation

Species: New Zealand White Rabbits

Results: Isodecyl benzoate produced slight to moderate erythema and edema reactions during the study..

Method: In accordance with USEPA Guidelines for Testing Pesticides and Toxic Substances, Guideline 81-5, 1982, and consistent with OECD Guidelines. Approximately 0.5 ml of neat material was applied to the skin of 3 male and 3 female rabbits, semi-occluded, for 4 hours. Measurements of edema and erythema were subsequently taken at 0 minutes, 4 hours, 24 hours, 48 hours, 72 hours and 96 hours after exposure.

Test Substance: Isodecyl benzoate, purity unknown.

Remarks: The primary dermal irritation scores were 1.7 (4 hours), 0.3 (24 hours), 1.0 (48 hours),. 1.0 (72 hours) and 0.5 (96 hours). The primary dermal irritation score is the total dermal irritation score for all the animals (erythema and edema) divided by the number of test sites (6) at each observation period. The material produced slight-to-moderate erythema and edema but is not classified as a skin irritant according to OECD guidelines.

Reliability: [1] Valid without Restriction

Reference: Hazleton Laboratories of America, Inc. "Primary Dermal Irritation Study of Isodecyl Benzoate in Rabbits." Report No. HLA 70504075, August 25, 1987.

(2) Eye Irritation

Type: Primary Eye Irritation

Species: New Zealand White Rabbits (male and female)

Result: The test material produced only slight to moderate conjunctival irritation during the study

Method: According to USEPA Guidelines for Testing Pesticides and Toxic Substances, Guideline 81-4, 1982, and consistent with OECD Guidelines. Each of the 6 rabbits received 0.1 ml of the neat test material placed on the everted lower lid of one eye, with the contralateral eye serving as the untreated control. The upper and lower lids were gently held together for one second to prevent loss of material and then released. The eyes of the rabbits remained unflushed. Observations for ocular irritation were done at 1, 24, 48 and 72 hours after treatment. At the 72-hour reading, sodium fluorescein was used to detect possible corneal injury. Irritation was graded and scored according to the Draize technique.

Test Substance: Isodecyl benzoate, purity unknown.

Remarks: The Primary Eye Irritation Score is the total eye irritation score for all animals divided by the number of animals (6) at each observation period. In this study, scores were 4.3 (1 hour), 4.3 (24 hours), 0.0 (48 hours) and 0.0 (72 hours). No corneal or iridic irritation was observed in any animal. The test material produced only slight to moderate conjunctival irritation but is not classified as an eye irritant according to OECD guidelines.

Reliablity: [1] Valid without Restrictions

Reference: Hazleton Laboratories of America, Inc. "Primary Eye Irritation Study of Isodecyl Benzoate in Rabbits." Report No. HLA 70504076, August 25, 1987.

C. SENSITIZATION

(1) Preferred Result

Type: Maximization Test

Species: Dunkin-Hartley Guinea Pigs (male)

Result: Isodecyl benzoate did not produce evidence of skin sensitization (delayed contact hypersensitivity) in the maximization test in guinea pigs.

Classification: Isodecyl benzoate does not require labeling with the risk phrase R43 "may cause sensitization by skin contact" in accordance with Council Directive 79/831/EEC Annex VI, Part II (D) as described in

Method: In compliance with EEC Methods for the Determination of Toxicity, Annex of Directive 92/69/EEC (OJ No. L38A, 29.12.92), Part B, Method B.6. Skin Sensitization. The method used was the guinea pig maximization test described by Magnusson, B. and A.M. Kligman. "Allergic Contact Dermatitis in the Guinea Pig: Identification of Contact Allergens," C.C. Thomas, Springfield, Illinois, USA, 1970.

Test Substance: Isodecyl Benzoate with a purity of 98.2% active ingredient

Vehicle: Alembicol D (a product of coconut oil supplied by Alembic Products, Saltney, Chester, England)

Remarks: Isodecyl benzoate, on the basis of preliminary studies, was tested as a 20% solution in Alembicol D in the intradermal induction phase, as neat material in the topical application phase, and as a 50% solution in Alembicol D in the challenge application. Ten test and 5 control guinea pigs were used in this study.

GLP: Yes [X] No [ ] ? [ ]

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Life Sciences, Ltd. "Benzoflex 131 (Isodecyl Benzoate): Skin Sensitization in the Guinea Pig." Report No. VCL 222/952365/55, November 29, 1995.

(2) Supporting Data

Type: Modified Buehler Test

Species: Dunkin-Hartley Guinea Pigs (male)

Result: Not an allergic skin sensitizer

Method: In accordance with USEPA Guideline for Testing Pesticides and Toxic Substances, Guideline 81-6, 1982. The test method used was the modified Buehler Test as described by E.V. Buehler and H.L. Ritz. "Planning, Conduct and Interpretation of Guinea Pig Sensitization Patch Tests," Current Concepts in Cutaneous Toxicity, p.28, 1980, and by E.V. Buehler. "Delayed Contact Hypersensitivity in the Guinea Pig." Arch. Dermatol. 91: 171-175, 1965.

Test Substance: Isodecyl benzoate, purity unknown

Vehicle: Mineral oil

Remarks: In the induction phase, isodecyl benzoate was applied topically as the neat material for a 6-hour period, one application a week for 3 weeks, to 10 guinea pigs. Two weeks later, the animals were challenged topically with isodecyl benzoate (25% w/v mixture in mineral oil). At the time of challenge, 10 naive (previously untreated) control animals were also treated with a challenge application of the same test material. Four positive controls were also used-0.3% DNCB for induction phase, 0.1% DNCB in the challenge phase. During the induction

phase, dermal irritation ranging from slight-to-moderate was seen. There was no evidence of delayed contact hypersensitivity.

GLP: Yes [X] No [ ] ? [ ]

Reliability: [1] Valid without Restrictions

Reference: Hazleton Laboratories of America, Inc. "Dermal Sensitization Study of Isodecyl Benzoate in Guinea Pigs (Closed Patch Technique)," Report No. HLA 70504077, February 1, 1988.

D. REPEATED DOSE TOXICITY

Species/Strain: Sprague-Dawley (Crl: CD^{R} BR VAF PLUS^{R}) Rats (male and female); 8 rats/sex/dose

Route of Administration: Oral Gavage

Exposure Period: 28 consecutive days.

Frequency of Treatment: Once a day

Post-Observation Period: None

Doses: 0, 15, 150 and 1000 mg/kg/day as an emulsion in corn oil

Controls: Corn oil alone at a equivalent dose volume (5ml/kg/day)

Method: In accordance with an Annex to Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part B, Method B.7 and consistent with OECD Guideline No. 407, 1981.

Results: NOEL=15mg/kg/day
NOAEL=150mg/kg/day
LOEL=1000mg/kg/day

Toxicologically significant effects occurred at the highest dose tested (1000 mg/kg/day). Behavioral changes were seen in rats and included altered appearance, palpbral closure in the area, tremors, increased hindlimb grip strength and increased hindlimb splay. Blood chemistry changes were unremarkable except for lower glucose levels in both sexes of rats. Higher liver (males and females) and kidney (males) weights were also noted. Histopathological examination showed only slight liver changes (increased hepatocyte enlargement in centrilobular area) in both sexes and kidney changes (eosinophilic intracytoplasmic droplets) in male rates (even at 150 mg/kg). However, the latter kidney change is specific to male rats and not relevant to man. There were no adverse effects relative to body weight, food and water consumption, hematology, and biochemistry.

Test Substance: Isodecyl benzoate with a purity of 95 to 99% active ingredient

Remarks: A functional observational battery (FOB) was performed on all animal once during acclimatization, once during Week 2 and once during Week 4. Blood samples for hematology and blood chemistry evaluation were taken from 5 rats/sex/dose on Day 28. Five male and 5 female rats from each group were sacrificed and examined macroscopically on Day 30; remaining animal were killed and discarded. Histopathologic examination included adrenals, heart, kidneys, liver, lungs, ovaries, spleen, testes, and any macroscopic anomalies.

GLP: Yes [X] No [ ] ? [ ]

Reliability: [2] Valid with restrictions
(The study was only 28 days in duration.)

Reference: Huntingdon Research Centre, Ltd. "Isodecyl Benzoate: Twenty-Eight Day Oral Toxicity Study in the Rat with Functional Observational Battery." Report No. VCL 206/942848, February 9, 1995.

E. GENETIC TOXICITY *IN VITRO*

(1) Bacterial Test

(a) Preferred Study
Type: Bacterial Reverse Point-Mutation Assay

System of Testing: Standard plate method using four *Salmonella typhimurium* strains (TA 98, TA 100, TA 1535, TA 1537) and one strain of *Escherichia coli* (WP2 uvrA trp)

Concentrations: 50 to 5000 µg/plate (preliminary toxicity tests)
312.5 to 5000 µg/plate (final tests)

Metabolic Activation: In the presence and absence of liver preparations from Aroclor 1254-induced rats

Results: No evidence of mutagenicity in these bacterial systems

Method: In compliance with OECD Guidelines No. 471 (*Salmonella typhimurium*) and No. 472 (*Escherichia coli),* 1983.

Test Substance: Isodecyl benzoate with a purity of 98.2% active ingredient

Remarks: The test substance was diluted in DMSO which was also used as the negative control (with activation). Positive controls were also used with (2-AA) and without (ENGG, 9-AC, and 2-NF) metabolic activation. Each test was run in duplicate.

GLP: [X] Yes [ ] No [ ] ?

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre, Ltd. "Isodecyl Benzoate: Bacterial Mutation Assay." Report No. VCL 225/960366, July 3, 1996.

(b) Supporting Data
Type: Bacterial Reverse Point-Mutation Assay

System of Testing: Standard plate method using 5 *Salmonella typhimurium* strains (TA 98, TA 100, TA 1535, TA 1537 and TA 1538)

Concentrations: 10 to 10,000 ug/plate (preliminary toxicity study); 667 to 10,000 ug/plate (final tests)

Metabolic Activation: In the presence and absence of liver preparations from Aroclor 1254-induced rats

Results: No evidence of mutagenicity in any of the 5 tester strains

Method: In accordance with OECD Guidelines and using methods described by Ames, B.N., McCann, J. and E. Yamasaki. Methods for Detecting Carcinogens and Mutagens with the *Salmonella*/Mammalian Microsome Mutagenicity Test, Mutat. Res. 31: 347-364, 1975, and by deSerres, F.J. and M.D. Shelby. The *Salmonella*/Mutagenicity Assay: Recommendations, Science 203: 563-565, 1979, and by Maron, D.M. and B.N. Ames. Revised Methods for the *Salmonella* Mutagenicity Test, Mutat. Res. 113: 173-215, 1983.

Test Substance: Isodecyl benzoate, purity unknown.

Remarks: The test substance was diluted in acetone which was also used as a vehicle control. Positive controls were also used with (2-AA) and without (2-NF, SA, 9-AC) metabolic activation. All positive controls, vehicle controls and test article doses were plated in triplicate.

GLP: [X] Yes [ ] No [ ] ?

Reliability: [2] Valid with Restrictions.
(Only one main mutation test was performed. The preliminary toxicity tests were run with only one strain of *Salmonella typhimurium).*

Reference: Microbiological Associates, Inc. "*Salmonella*/Mammalian-Microsome Plate Incorporation Mutagenicty Assay, "Laboratory Study Number T5559.501, July 1, 1987.

(2) Non-Bacterial *In Vitro* Test

Type: Chromosome Aberration Assay

System of Testing: Cultured human lymphocytes

Concentrations: 19.5, 39.1 and 78.1 ug/ml (without S-9); 625, 2500 and 5000 ug/ml (with S-9)

Metabolic Activation: In the presence and absence of liver preparations from Aroclor 1254-induced rats

Results: No evidence of clastogenic activity, with or without metabolic activation

Method: In compliance with OECD Guideline Test No. 473, 1983.

Test Substance: Isodecyl benzoate at a purity of >98% active ingredient

Remarks: In the absence of S-9 mix, isodecyl benzoate caused no statistically significant increase in the proportion of metaphase figures containing chromosomal aberrations at any dose level when compared to the solvent control (DMSO). In the presence of S-9 mix, it caused an increase within historical limits in the proportion of metaphase figures containing chromosomal aberrations at 5000 ug/plate (18-hr harvest) in the first of two tests, but not in the second test at either harvest time (18 hours or 32 hours). Following consultation with regulatory agencies, and additional solubility studies, a third test (with S9) at 4 test article concentrations from 100 tp 312.5 µg/ml was conducted. Isodecyl benzoate caused no statistically significant increase in the proportion of metaphase figures containing chromosomal aberrations at any dose level. Positive control compounds (CP with S9, EMS without S9) in all three tests caused large, statistically significant increases in the proportion of aberrant cells. On the basis of 3 separate tests, it was concluded that isodecyl benzoate showed no evidence of clastogenic activity.

GLP: [X] Yes [ ] No [ ] ?

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Life Sciences, Ltd. "Isodecyl Benzoate: Metaphase Chromosome Analysis of Human Lymphocytes Cultured *In Vitro,* Report No. VCL 216/248/950137, November 26, 1997.

F. GENETIC TOXICITY *IN VIVO*

Type: Micronucleus Study

Species/Strain: Swiss SPF CD-1 Outbred Mice

Sex: Male and female

Route of Administration: Intraperitoneal injection

Dose: 1280 mg/kg body weight (maximum tolerated dose)

Sacrifice/Sampling Intervals: 24, 48 and 72 hours

Results: Isodecyl benzoate showed no evidence of causing chromosome damage when administered intraperitoneally to mice in this *in vivo* mouse micronucleus assay

Effect on Mitotic Index or P/N Ratio: Slight but statistically significant decreases in the ratio of polychromatic to normochromatic erythrocytes were seen at the 48-hour and 72-hour sampling times after treatment of the mice with isodecyl benzoate.

Genotoxic Effects: not an *in vivo* mutagen

Method: Based on the recommendations of OECD Guideline No. 474, 1983, and the EEC Annex to Directive 92/69/EEC, 1992, and USEPA (TSCA) Guideline No. 798.5395, 1997.

GLP: Yes [X] No [ ] ? [ ]

Test Substance: Isodecyl benzoate at a purity of 98% active ingredient

Remarks: A vehicle control (1% methylcellulose) and a positive control (mitomycin C) were also used in this study. Five male and 5 female mice were used to test isodecyl benzoate, the vehicle control and the positive control, respectively. Isodecyl benzoate had no chromosome-damaging (clastogenic) effects nor did it cause any impairment of chromosome distribution in mitosis.

Reliability: [1] Valid without Restrictions

Reference: Huntingdon Research Centre, Ltd. " Isodecyl Benzoate: Mouse Micronucleus". Report No. VCL 207/941604, February 7, 1995.

G. CARCINOGENICITY – No Information

H. TOXICITY TO REPRODUCTION

Type: 28-Day Oral Toxicity Study

Species/Strain: Sprague-Dawley Crl CD^{R}BR VAF; PLUS^{R}Rats (Male and Female)

Route of Administration: Oral gavage

Exposure Period: 28 days

Frequency of Treatment: Once a day by gavage

Duration of Test: 28 days

Doses: 0, 15, 150 and 1000 mg/kg/day

Control Group: Yes (corn oil alone)

Method: In accordance with OECD Guideline No. 407, May 12, 1981. After 29 days of treatment (Day 30), 5 rats/sex/group were sacrificed by CO_2 asphyxiation. The following reproductive organs from each animal undergoing *post mortem* examination were dissected free of fat and weighed: epididymides, ovaries, prostate, seminal vesicles and testes. Testes and epididymides were weighed individually as left and right. For microscopic examination, a transverse section of each testis (left and right) and a full longitudinal section of each epididymis (left and right) were cut as near as possible to 2 mμ and stained with Periodic Acid Schiff-Hematoxylin. Microscopic examination of the testes was made with reference to the stages of the cycle of the seminiferous epithelium. Microscopic examination of prepared slides from ovaries and testes including epididymis was carried out for 5 rats/sex/dose for the control and high dosage groups only.

Test Substance: Isodecyl benzoate at a purity of 95 to 99% active ingredient.

Results: Statistically significant lower than control ovary (body weight adjusted) weights were seen in the high-dose females but were not considered treatment-related. All other reproductive organ weights from high-dose rats were similar to controls and the gross pathological examination was unremarkable. In addition, the microscopic examination of ovaries and testes (including epididymis) from high-dose rats was unremarkable.

GLP: Yes [X] No [ ] ? [ ]

Remarks: An adequate repeat-dose general toxicity study (without a mating trial), such as this 28-day study, in association with a developmental toxicity study (See Section 5.1), should be considered acceptable to fulfill the reproductive/developmental endpoints for both the OECD/SIDS Program and the HPV Program.

Reliability: [2] Valid with Restrictions.

Reference: Huntingdon Research Centre, Ltd. "Twenty-Eight Day Oral Toxicity Study in the Rat with Functional Observational Battery". Report No. VCL 206/942848, February 9, 1995.

I. DEVELOPMENTAL TOXICITY/TERATOGENICITY

Type: Developmental Toxicity Study

Species/Strain: Sprague-Dawley Crl:CD^{R}BR pregnant female rats

Route of Administration: Oral gavage

Exposure Period: Days 6 through 15 of gestation

Frequency of Treatment: Once a day by oral gavage

Duration of Test: Up to Day 20 of gestation when a laparohysterectomy was performed on all animals

Doses: 30, 300 and 1000 mg/kg at a dose volume of 5 ml/kg; 25 rats/ dose level

Control Group: Yes (25 rats given corn oil at a purity of 98% active ingredient)

Method: In accordance with OECD Guideline No. 414, 198_.

Test Substance: Isodecyl benzoate at a purity of 98% active ingredient

Results: No adverse clinical signs related to treatment were seen at any dose. Minimal adverse effects in this study were seen only at the 1000 mg/kg dose. A decrease in body weight gain in maternal rats was noted during gestation days 6 through 9 only but food consumption was unaffected throughout the study. No treatment-related internal findings were observed at necropsy. The only adverse effects of treatment on the developing fetus were a decrease in mean fetal body weight and a reduction in the incidence of cervical centrum no. 1 ossified (both of which are suggestions of developmental retardation in the fetuses). No other treatment-related malformations or developmental variations were observed at any dose level. A dose level of 300 mg/kg was considered to be the NOAEL for maternal toxicity and developmental toxicity.

GLP: Yes [X] No [ ] ? [ ]

Remarks: A dose of 1000 mg/kg isodecyl benzoate was the LOAEL for this study for both maternal toxicity (transient mean body weight loss) and developmental toxicity (decrease in mean fetal body weight and in the incidence of cervical centrum no. 1 ossified). A dose level of 300 mg/kg was considered to be the NOAEL for both maternal and developmental toxicity. Isodecyl benzoate does not pose a unique hazard for the developing fetus. A dose range-finding study in 8 rats/dose at dose levels of 25, 100, 400, 700 and 1000 mg/kg conducted in the same laboratory (WIL 1994) provided the basis for dose selection in this study. In the latter study, post-implantation loss was increased and mean fetal body weight was decreased in the 1000 mg/kg group. The only external malformation seen was craniorachischisis in one fetus of the 700 mg/kg group. Maternal toxicity (decreased body weight gain) was seen at both 1000 and 700 mg/kg. No developmental toxicity was observed in the 25, 100, 400 or 700 mg/kg groups.

Reliability: [1] Valid without Restrictions

Reference: WIL Research Laboratories, Inc. A Developmental Toxicity Study of Isodecyl Benzoate in Rats. Laboratory Study No. WIL-15218, February 10, 1995.

J. **ADDITIONAL REMARKS** - None

K. **EXPERIENCE WITH HUMAN EXPOSURE** – There have been no adverse effects reporting during the manufacture or use of this product during the life of the product. It is handled in primarily closed systems with minimal opportunity for exposures. There have been no adverse effects associated with the incorporation of this product in end products such as caulks or sealants.

6.0 **REFERENCES**

Study references are cited at the end of the section describing each of the tox studies.